Demo Analysis of Remdesivir Trial

David Darmon

2 May 2020

Timestamp 20:44 of https://bloggingheads.tv/videos/58839?in=20:44.

What you said isn't quite right. The 5% significance level means that **if** there were no difference in mortality rates between the treatment and control groups, **then** there is a 5% chance of rejecting the null hypothesis of no difference between the treatment and control groups. That *does* mean that **if** there were no difference, then there is a 95% chance of **not** rejecting the null hypothesis. But that **does not** mean there is a 95% chance of the true difference being different from 0. In fact, under the frequentist model inherent in this type of hypothesis testing, making a probabilistic claim about the true difference does not make sense: either the difference is different from zero or it is not.

The main confusion comes from misinterpreting the P-value, in this case the P-value of 0.059 for the observed difference in the death rates:

https://www.niaid.nih.gov/news-events/nih-clinical-trial-shows-remdesivir-accelerates-recovery-advanced-covid-19

The P-value **is not** Prob(Null Hypothesis Is True Given Evidence), and thus one minus the P-value **is not** Prob(Alternative Hypothesis Is True Given Evidence). The P-value is just the probability of a difference as extreme or more extreme than the observed difference in mortality rates if there really is no difference in the underlying mortality rates.

You are also confusing confidence intervals with significance tests. They are related (you can always get a confidence interval by inverting a significance test, and vice versa), but conceptually distinct.

We can (and should) use confidence intervals to get a better idea about the effect of Remdesivir relative to the control treatment.

Data for the Trial

```
n.tot <- 1063 # Total sample size

# Assuming equal allotment to each arm of the clinical trial.
# This seems if-y.

n1 <- n.tot / 2 - 0.5
n2 <- n.tot / 2 + 0.5

p1 <- 0.116 # Mortality rate in control group
p2 <- 0.08 # Mortality rate in remdesivir

# The approximate number of deaths in each group.

x1 <- n1*p1 # control
x2 <- n2*p2 # Remdesivir
```

Test for difference of two proportions.

```
prop.test(x = c(x1, x2), n = c(n1, n2), correct = TRUE)
```

```
##
##  2-sample test for equality of proportions with continuity correction
##
## data:  c(x1, x2) out of c(n1, n2)
## X-squared = 3.5002, df = 1, p-value = 0.06136
## alternative hypothesis: two.sided
## 95 percent confidence interval:
##  -0.001564698  0.073564698
## sample estimates:
## prop 1 prop 2
##  0.116  0.080
```

The 95% confidence interval indicates that the effect of remdesivir ranges from a large decrease in the mortality rate (by as much as 7.35 percentage points) to a small increase in the mortality rate (by as much as 0.16 percenage points).

Odds Ratio-based Analysis

```
(p2/(1 - p2))/(p1/(1-p1))
```

```
## [1] 0.6626687
```

This means the best estimate is that the odds of dying in the treatment group is 66.3% of the odds of dying in the control group.

Note that this **does not** mean that the **risk** (probability) of dying in the treatment group is 66.3% of the risk of dying in the control group.

For example, if the true risk of dying were 12% in the control group, then the risk of dying in the treatment group would be:

$$\begin{aligned}\rho &= \frac{p_T/(1-p_T)}{p_C/(1-p_C)} \\ &= p_T/(1-p_T)/\omega_C\end{aligned}$$

$$\frac{p_T}{1-p_T} = \omega_C\rho \implies p_T = \frac{\omega_C\rho}{\omega_C\rho+1} \neq \rho p_C$$

```
omega.c <- 0.12/(1-0.12)
rho <- 0.663

(omega.c*rho)/(omega.c*rho+1)
```

```
## [1] 0.082913
```

```
rho*0.12
```

```
## [1] 0.07956
```

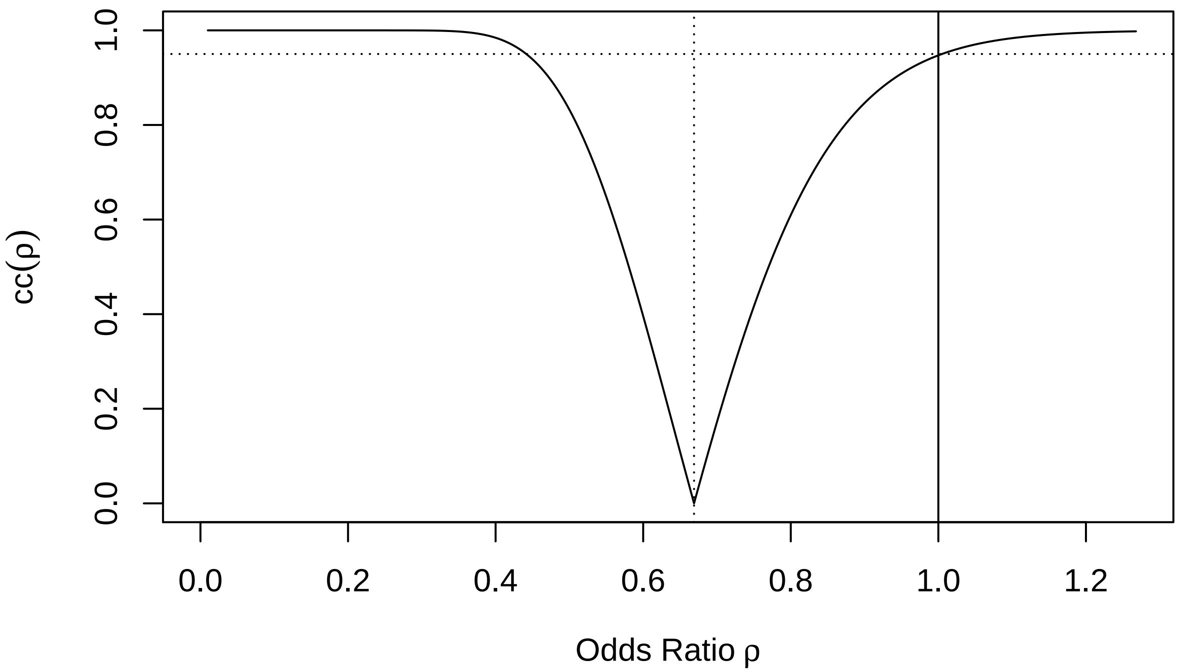
Confidence Curve for Odds Ratio

```r
library(confcurve)

confcurve.or(ys = ceiling(c(x1, x2)), ns = ceiling(c(n1, n2)))
```

```
## $ci
##             lr       rr
## [1,] 0.4415663 1.004897
##
## $or.median.est
## [1] 0.6689309
```

```r
abline(h = 0.95, lty = 3)
```



The confidence interval based on the odds ratio indicates that there is anywhere from a (100% - 44.16%) = 55.84% decrease to a (100.49% - 100%) = 0.49% increase in the odds of dying using Remdesivir compared to the control. Again, this is in terms of the **odds**, not the **risk** of dying.